

10/816,544

FILE COVERS 1907 - 2 Feb 2009 VOL 150 ISS 6  
FILE LAST UPDATED: 1 Feb 2009 (20090201/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

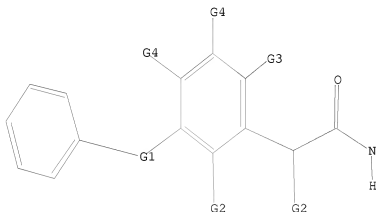
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L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



G1 NH,O

G2 X,OH,H

G3 CN,Ak

G4 OH,C,X,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

10/923,271

FULL SEARCH INITIATED 11:42:41 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 4530 TO ITERATE

100.0% PROCESSED 4530 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.02

L2 0 SEA SSS FUL L1

L3 0 L2

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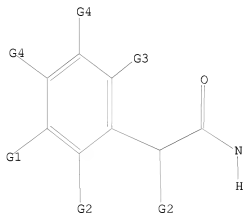
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L4 STRUCTURE UPLOADED

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L4 HAS NO ANSWERS

L4 STR



G1 NH,O

G2 X,CH,H

G3 CN,Ak

G4 OH,C,X,H

Structure attributes must be viewed using STN Express query preparation.

=> s l4 full

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

10/923,271

FULL SEARCH INITIATED 11:43:47 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 87422 TO ITERATE

100.0% PROCESSED 87422 ITERATIONS  
SEARCH TIME: 00.00.04

126 ANSWERS

L5 126 SEA SSS FUL L4

L6 18 L5

=> s 16 and py<2003  
22983121 PY<2003  
L7 11 L6 AND PY<2003

=> d 1-11 ibib abs hitstr

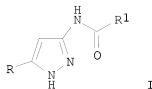
L7 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:374223 CAPLUS  
DOCUMENT NUMBER: 144:412501  
TITLE: Preparation of 3(5)-acylaminopyrazole derivatives for  
use as therapeutic agents, particularly antitumor  
agents  
INVENTOR(S): Pevarello, Paolo; Orsini, Paolo; Traquandi, Gabriella;  
Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha  
A.; Pierce, Betsy S.; Brasca, Maria Gabriella  
PATENT ASSIGNEE(S): Pharmacia Italia S.p.A., Italy; Pharmacia & Upjohn  
Company LLC  
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 372,831,  
abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

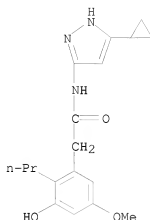
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 7034049	B1	20060425	US 2002-48486	20020501
WO 2001012189	A1	20010222	WO 2000-US6699	20000505 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6218418	B1	20010417	US 2000-667603	20000922 <--
PRIORITY APPLN. INFO.:			US 1999-372831	B2 19990812
			WO 2000-US6699	W 20000505
			US 2000-560400	A1 20000428
OTHER SOURCE(S):	MARPAT 144:412501			
GI				

ToH

02/02/2009



- AB Compds. (e.g., N-(5-cyclopropyl-1H-pyrazol-3-yl)-2,2-diphenylacetamide) which are 3-amino-pyrazole derivs. represented by formula I (wherein R = C3-C6 cycloalkyl group optionally substituted by a straight or branched C1-C6 alkyl or arylalkyl group; R1 = a straight or branched C1-C6 alkyl, C2-C4 alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, arylalkyl, arylcarbonyl, aryloxyalkyl or arylalkenyl group, each of which may be optionally further substituted) are claimed. A process for preparing the 3-aminopyrazole derivs. comprises: (a) reacting  $\text{RCO}_2\text{R}_2$  ( $\text{R}_2 = \text{alkyl}$ ), with MeCN in the presence of a basic agent, to obtain  $\text{RC(O)CH}_2\text{CN}$ ; (b) reacting  $\text{RC(O)CH}_2\text{CN}$  with hydrazine hydrate to obtain an 3-amino-5-R-1H-pyrazole; (c) oxidizing the 3-amino-5-R-1H-pyrazole to obtain the nitro analog; (d) reacting the nitro compound with tert-butoxycarbonyl anhydride (Boc<sub>2</sub>O) to obtain the N-Boc derivative which was reduced; (e) reacting this amino compound with  $\text{R1C(O)X}$  ( $\text{X} = \text{OH}$  or a suitable leaving group) to obtain the N1-Boc-protected I; and (g) hydrolyzing this intermediate in an acidic medium to obtain I. The compds. are useful for the treatment of cancer, cell proliferative disorders, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative diseases (no data is given). Pharmaceutical compns. containing I are also claimed.
- IT 326825-31-4P, N-(5-Cyclopropyl-1H-pyrazol-3-yl)-2-(5-methoxy-3-hydroxy-2-propylphenyl)acetamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 3(5)-acylaminopyrazole derivs. for use as therapeutic agents, particularly antitumor agents)
- RN 326825-31-4 CAPLUS
- CN Benzeneacetamide, N-(5-cyclopropyl-1H-pyrazol-3-yl)-3-hydroxy-5-methoxy-2-propyl- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2002:275956 CAPLUS  
 DOCUMENT NUMBER: 136:294655  
 TITLE: Aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl- substituted phenyl acetamides as protease inhibitors  
 INVENTOR(S): Pan, Wenxi; Lu, Tianbao; Markotan, Thomas P.; Tomczuk, Bruce E.  
 PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 118 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028825	A2	20020411	WO 2001-US31249	20011005 <--
WO 2002028825	A3	20020613		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2423883	A1	20020411	CA 2001-2423883	20011005 <--
AU 2002011464	A1	20020415	AU 2002-11464	20011005 <--
US 20020061872	A1	20020523	US 2001-971000	20011005 <--
US 6521663	B2	20030218		
EP 1324981	A2	20030709	EP 2001-979513	20011005
EP 1324981	B1	20060823		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

HU 2003003149	A2	20040128	HU 2003-3149	20011005
BR 2001014263	A	20040302	BR 2001-14263	20011005
JP 2004510759	T	20040408	JP 2002-532411	20011005
ZA 2003003091	A	20040722	ZA 2003-3091	20011005
NZ 525438	A	20040924	NZ 2001-525438	20011005
CN 1568307	A	20050119	CN 2001-818254	20011005
CN 1315803	C	20070516		
AU 2002211464	B2	20060622	AU 2002-211464	20011005
AT 337299	T	20060915	AT 2001-979513	20011005
ES 2269474	T3	20070401	ES 2001-979513	20011005
US 20030073833	A1	20030417	US 2002-262871	20021003
US 6900231	B2	20050531		
NO 2003001390	A	20030603	NO 2003-1390	20030326
MX 2003002998	A	20040212	MX 2003-2998	20030404
IN 2003KN00504	A	20050311	IN 2003-KN504	20030423
HK 1058032	A1	20070316	HK 2004-100042	20040102
US 20050159457	A1	20050721	US 2005-32297	20050110
PRIORITY APPLN. INFO.:			US 2000-238132P	P 20001006
			US 2001-971000	A3 20011005
			WO 2001-US31249	W 20011005
			US 2002-262871	A1 20021003

OTHER SOURCE(S): MARPAT 136:294655

AB The compds. of the invention are potent inhibitors of proteases, especially trypsin-like serine proteases, such as thrombin and factor Xa. Compns. for inhibiting loss of blood platelets, inhibiting formation of blood platelet aggregates, inhibiting formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation are described. Other uses of compds. of the invention are as anticoagulants either embedded in or phys. linked to materials used in the manufacture of devices used in blood collection, blood circulation, and blood storage, such as catheters, blood dialysis machines, blood collection syringes and tubes, blood lines and stents. Addnl., the compds. can be detectably labeled and employed for in vivo imaging for thrombi. The 11 title compds. prepared have Ki values for human thrombin of between 0.0028 and 20µM. Among the 11 title compds. prepared by standard methods were 98% N-[2-(amidinoaminoxy)ethyl]-2-{3-[(2,2-difluoro-2-phenylethyl)amino]-6-chloro-2-fluorophenyl}acetamide, 99% N-[2-(amidinoaminoxy)ethyl]-2-{3-[2,2-difluoro-2-(4-fluoronaphthyl)ethylamino]-6-chloro-2-fluorophenyl}acetamide and 100% N-[2-(guanidinoxy)ethyl]-2-[2-chloro-5-(benzylsulfonylamino)phenyl]acetamide.

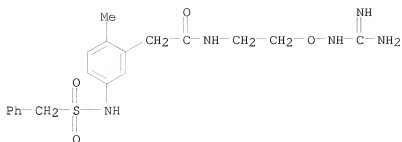
IT 409081-63-6P 409081-64-7P 409081-65-8P  
 409081-66-9P 409081-67-0P 409082-40-2P  
 409082-41-3P 409082-42-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation of aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl-substituted phenylacetamides as anticoagulants)

RN 409081-63-6 CAPLUS

CN Benzeneacetamide, N-[2-[(aminoiminomethyl)amino]oxyethyl]-2-methyl-5-[[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

10/923,271

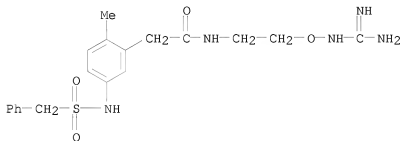


RN 409081-64-7 CAPLUS  
 CN Benzeneacetamide, N-[2-[[[(aminoiminomethyl)amino]oxy]ethyl]-2-methyl-5-  
 [[[(phenylmethyl)sulfonyl]amino]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX  
 NAME)

CM 1

CRN 409081-63-6

CMF C19 H25 N5 O4 S



CM 2

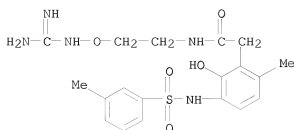
CRN 76-05-1

CMF C2 H F3 O2



RN 409081-65-8 CAPLUS  
 CN Benzeneacetamide, N-[2-[[[(aminoiminomethyl)amino]oxy]ethyl]-2-hydroxy-6-  
 methyl-3-[[[(3-methylphenyl)sulfonyl]amino]-, hydrochloride (1:1) (CA  
 INDEX NAME)

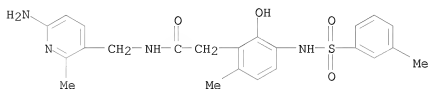
10/923,271



● HCl

RN 409081-66-9 CAPLUS

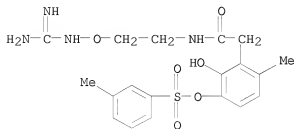
CN Benzeneacetamide, N-[(6-amino-2-methyl-3-pyridinyl)methyl]-2-hydroxy-6-methyl-3-[(3-methylphenyl)sulfonyl]amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 409081-67-0 CAPLUS

CN Benzenesulfonic acid, 3-methyl-, 3-[2-[[2-[(aminoiminomethyl)amino]oxy]ethyl]amino]-2-oxoethyl]-2-hydroxy-4-methylphenyl ester, hydrochloride (1:1) (CA INDEX NAME)



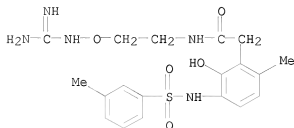
● HCl

RN 409082-40-2 CAPLUS

CN Benzeneacetamide, N-[2-[(aminoiminomethyl)amino]oxy]ethyl]-2-hydroxy-6-

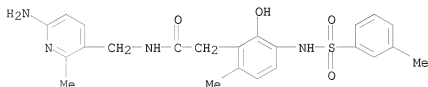


methyl-3-[[ (3-methylphenyl)sulfonyl]amino]- (CA INDEX NAME)



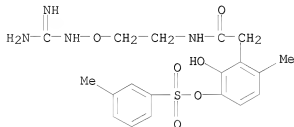
RN 409082-41-3 CAPLUS

CN Benzeneacetamide, N-[(6-amino-2-methyl-3-pyridinyl)methyl]-2-hydroxy-6-methyl-3-[[ (3-methylphenyl)sulfonyl]amino]- (CA INDEX NAME)



RN 409082-42-4 CAPLUS

CN Benzenesulfonic acid, 3-methyl-, 3-[2-[[2-[(aminoininomethyl)amino]oxy]ethyl]amino]-2-oxoethyl]-2-hydroxy-4-methylphenyl ester (CA INDEX NAME)



IT 409082-17-3P 409082-19-5P 409082-26-4P

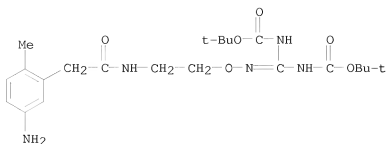
409082-36-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl-substituted phenylacetamides as anticoagulants)

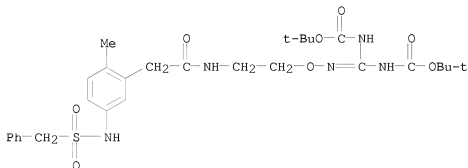
RN 409082-17-3 CAPLUS

CN 5-Oxa-2,4,8-triazadec-2-enoic acid, 10-(5-amino-2-methylphenyl)-3-[[ (1,1-dimethylethoxy)carbonyl]amino]-9-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)



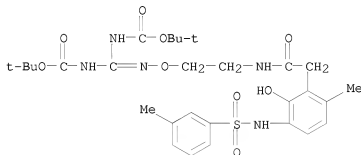
RN 409082-19-5 CAPLUS

CN 5-Oxa-2,4,8-triazadec-2-enoic acid,  
3-[[ (1,1-dimethylethoxy)carbonyl]amino]-10-[2-methyl-5-  
[[ (phenylmethyl)sulfonyl]amino]phenyl]-9-oxo-, 1,1-dimethylethyl ester  
(CA INDEX NAME)



RN 409082-26-4 CAPLUS

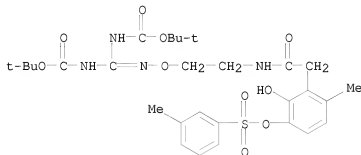
CN 5-Oxa-2,4,8-triazadec-2-enoic acid,  
3-[[ (1,1-dimethylethoxy)carbonyl]amino]-10-[2-hydroxy-6-methyl-3-[[ (3-  
methylphenyl)sulfonyl]amino]phenyl]-9-oxo-, 1,1-dimethylethyl ester (CA  
INDEX NAME)



RN 409082-36-6 CAPLUS

CN 5-Oxa-2,4,8-triazadec-2-enoic acid,  
3-[[ (1,1-dimethylethoxy)carbonyl]amino]-10-[2-hydroxy-6-methyl-3-[[ (3-

methylphenyl)sulfonyl]oxy]phenyl]-9-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:719012 CAPLUS

DOCUMENT NUMBER: 135:280431

TITLE: Photographic element and compound and process useful therewith

INVENTOR(S): Romanet, Robert F.; Vreeland, William B.; Harder, John W.; Brown, Christopher T.; Conley, Scott R.; Youngblood, Michael P.

PATENT ASSIGNEE(S): Eastman Kodak Company, USA

SOURCE: U.S., 52 pp.

CODEN: USXXAM

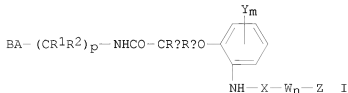
DOCUMENT TYPE: Patent

LANGUAGE: English

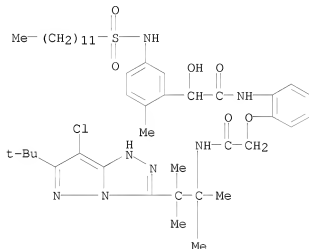
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6296997	B1	20011002	US 2000-707586	20001107 <--
EP 1205796	A2	20020515	EP 2001-204126	20011029 <--
EP 1205796	A3	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002162718	A	20020607	JP 2001-342355	20011107 <--
PRIORITY APPLN. INFO.:			US 2000-707586	A 20001107
OTHER SOURCE(S):	MARPAT 135:280431			
GI				



- AB The invention describes a silver halide photog. element containing a dye-forming bicyclic azole coupler having a phenoxy substituent containing an ortho substituent for better color rendition. The photog. element comprises a light-sensitive Ag halide emulsion layer having associated therewith a bicyclic azole dye-forming coupler compound (I) where BA = a bicyclic azole coupler nucleus with  $-(C(R1)(R2))P-$  bonded to a ring C in a non-coupling position of the coupler nucleus; p is 1 or 2, and each R1 and R2 is independently selected from H and a substituent group, provided that any 2 of R1 and R2 may join to form a ring; Ra and Rb are each independently selected from H and a substituent group, provided that substituent groups may join to form a ring; each Y is an independently selected substituent and m is 0-4; X is selected from the group consisting of  $-C(O)-$ ,  $-S(O)2-$ ,  $-S(O)-$ , and  $-P(O)(OH)-$ ; W is a connecting group having a chain of up to 4 atoms between X and Z, and n = 0 or 1; and (a) when n = 0, Z is  $-NHR5$  where R5 is H or a substituent, and (b) when n = 1, Z is selected from  $-OH$ ,  $-SO2NHR5$ , and  $-NHR6$  where R5 is H or a substituent group and R6 is a substituent bonded to  $-NH-$  by an electron withdrawing group in R6; provided that the ClogP value of the coupler compound is at least 5.0. The element provides improved color rendition.
- IT 363595-70-4  
 RL: NUU (Other use, unclassified); TEM (Technical or engineered material use); USES (Uses)  
 (photog. element containing dye-forming bicyclic azo coupler for better color reproduction)
- RN 363595-70-4 CAPLUS
- CN Benzeneacetamide, N-[2-[2-[[2-[7-chloro-6-(1,1-dimethylethyl)-1H-pyrazolo[5,1-c]-1,2,4-triazol-3-yl]-1,1,2-trimethylpropyl]amino]-2-oxoethoxy]phenyl]-5-[(dodecylsulfonyl)amino]- $\alpha$ -hydroxy-2-methyl- (CA INDEX NAME)

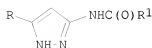


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

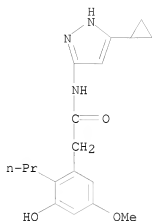
ACCESSION NUMBER: 2001:137023 CAPLUS  
 DOCUMENT NUMBER: 134:178552  
 TITLE: 3(5)-Acylaminopyrazole derivatives, process for their preparation and their use as antitumor agents  
 INVENTOR(S): Pevarello, Paolo; Orsini, Paolo; Traquandi, Gabriella; Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha A.; Pierce, Betsy S.; Brasca, Maria Gabriella  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn S.p.A., Italy; Pharmacia & Upjohn Company  
 SOURCE: PCT Int. Appl., 123 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012189	A1	20010222	WO 2000-US6699	20000505 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383555	A1	20010222	CA 2000-2383555	20000505 <--
AU 2000049714	A	20010313	AU 2000-49714	20000505 <--
EP 1202733	A1	20020508	EP 2000-931906	20000505 <--
EP 1202733	B1	20051005		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000013143	A	20020611	BR 2000-13143	20000505 <--
JP 2003507329	T	20030225	JP 2001-516535	20000505
EE 200200065	A	20030415	EE 2002-65	20000505
HU 2002003542	A2	20030528	HU 2002-3542	20000505
HU 2002003542	A3	20030728		
NZ 517237	A	20040227	NZ 2000-517237	20000505
AT 305782	T	20051015	AT 2000-931906	20000505
ES 2249270	T3	20060401	ES 2000-931906	20000505
US 6218418	B1	20010417	US 2000-667603	20000922 <--
NO 2002000684	A	20020403	NO 2002-684	20020211 <--
HR 2002000128	A1	20030430	HR 2002-128	20020212
MX 2002001498	A	20030721	MX 2002-1498	20020212
ZA 2002001511	A	20030311	ZA 2002-1511	20020222
BG 106480	A	20020930	BG 2002-106480	20020305 <--
US 7034049	B1	20060425	US 2002-48486	20020501
PRIORITY APPLN. INFO.:			US 1999-372831	A 19990812
			US 2000-560400	A1 20000428
			WO 2000-US6699	W 20000505
OTHER SOURCE(S):	MARPAT 134:178552			
GI				



I

- AB Compds. which are 3-acylamino-pyrazole derivs. (I; e.g. N-(5-cyclopropyl-1H-pyrazol-3-yl)-2,2-diphenylacetamide) wherein R is C3-C6 cycloalkyl group optionally substituted by a straight or branched C1-C6 alkyl or arylalkyl group; R1 is a straight or branched C1-C6 alkyl, C2-C4 alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, arylalkyl, arylcarbonyl, aryloxyalkyl or arylalkenyl group, each of which may be optionally further substituted as indicated in the description; or a pharmaceutically acceptable salt thereof, processes for their preparation and their therapeutic uses. The compds. are useful for the treatment of cancer, cell proliferative disorders, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative diseases, but no quant. test results are presented. The cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma. The cell proliferative disorder is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis glomerulonephritis and post-surgical stenosis and restenosis. The method of treatment provides tumor angiogenesis and metastasis inhibition, cell cycle inhibition or cdk/cyclin dependent inhibition, and treatment or prevention of radiotherapy-induced or chemotherapy-induced alopecia. A process for preparing the 3-aminopyrazole derivative or the pharmaceutically acceptable salt thereof, comprising: (a) reacting RCO2R2 (R2 = alkyl), with MeCN in the presence of a basic agent, to obtain RC(O)CH2CN; (b) reacting RC(O)CH2CN with hydrazine hydrate to obtain an 3-amino-5-R-1H-pyrazole; (c) oxidizing the 3-amino-5-R-1H-pyrazole to obtain the nitro analog; (d) reacting the nitro compound with tert-butoxycarbonyl anhydride (Boc2O) to obtain the N-Boc derivative; (e) reducing this BOC derivative to obtain the amino analog;
- (f) reacting this amino compound with R1C(O)X (X = OH or a suitable leaving group) to obtain the N1-Boc-protected I; and (g) hydrolyzing this intermediate in an acidic medium to obtain I. Other methods of preparation are also claimed.
- IT 326825-31-4P, N-(5-Cyclopropyl-1H-pyrazol-3-yl)-2-(5-methoxy-3-hydroxy-2-propylphenyl)acetamide  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (acylamino-pyrazole derivs., process for preparation and use as antitumor agents)
- RN 326825-31-4 CAPLUS
- CN Benzeneacetamide, N-(5-cyclopropyl-1H-pyrazol-3-yl)-3-hydroxy-5-methoxy-2-propyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2000:307678 CAPLUS  
 DOCUMENT NUMBER: 133:150300  
 TITLE: Leaving group effects in reductively triggered fragmentation of 4-nitrobenzyl carbamates  
 AUTHOR(S): Sykes, Bridget M.; Hay, Michael P.; Bohinc-Herceg, Dubravka; Helsby, Nuala A.; O'Connor, Charmian J.; Denny, William A.  
 CORPORATE SOURCE: Faculty of Medical and Health Sciences, Auckland Cancer Society Research Centre, The University of Auckland, Auckland, N. Z.  
 SOURCE: Perkin 1 (2000), (10), 1601-1608  
 CODEN: PERKF9; ISSN: 1470-4358  
 PUBLISHER: Royal Society of Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The rates and extent of release of a series of substituted anilines from 4-nitrobenzyl carbamates, following nitro group reduction by radiolytic, enzymic and chemical methods, are reported. The yield of released anilines decreased over the pH range 4-7, but was independent of the basicity of the leaving aniline. Detailed studies of the fragmentation of one example identified the 4-hydroxylamine as the key intermediate. At pH greater than 5 the released aniline I condenses with a reactive 4-iminoquinomethane intermediate to give amine II, thus depleting the measurable amount of aniline I released. At pH less than 5 the release of amine proceeds to completion. The efficiency of reductively triggered release of anilines (III; R=H, Me, OMe, SO<sub>2</sub>Me) varied with small changes in the leaving group, but this was not uniformly related to aniline basicity. The competing reaction of the released aniline I to form amine II lowers

the efficiency of release of I. This reaction occurs at the relatively high concns. (50  $\mu$ M) used in the study and indicates the released effector amine should be toxic at concns. considerably lower than 50  $\mu$ M. This highlights the need for prodrugs of very potent cytotoxic effectors to be used in tumor-directed nitroreductase enzyme-prodrug therapy.

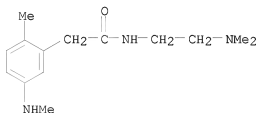
IT 287120-22-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(leaving group effects in reductively triggered fragmentation of 4-nitrobenzyl carbamates)

RN 287120-22-3 CAPLUS

CN Benzeneacetamide, N-[2-(dimethylamino)ethyl]-2-methyl-5-(methylamino)-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:354477 CAPLUS

DOCUMENT NUMBER: 130:352556

TITLE: Synthesis of substituted 3-amino-2-hydroxyphenylacetamide derivatives as enzyme inhibitors

INVENTOR(S): Semple, Joseph Edward; Lim-Wilby, Marguerita S.; Brunck, Terence K.

PATENT ASSIGNEE(S): Corvas International, Inc., USA

SOURCE: PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926920	A1	19990603	WO 1998-US25167	19981123 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				

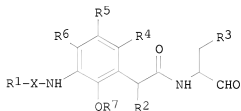


RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6011047	A	20000104	US 1997-980114	19971126 <--
US 6204384	B1	20010320	US 1997-979440	19971126 <--
AU 9916056	A	19990615	AU 1999-16056	19981123 <--

PRIORITY APPLN. INFO.: US 1997-979440 A 19971126  
 US 1997-980114 A 19971126  
 WO 1998-US25167 W 19981123

OTHER SOURCE(S): MARPAT 130:352556  
 GI



AB Peptide aldehydes I [X = SO<sub>2</sub>, NR'SO<sub>2</sub>, CO, OCO, NHCO, P(O)R'', or direct link (R' = H, alkyl, aryl, aralkyl; R'' = NHR', OR', R', SR')]; R1 = (un)substituted alkyl, cycloalkylalkyl, cycloalkyl, heterocycloalkyl, aryl, etc.; R2 = H, alkyl, alkenyl; R3 = HN:C(NH<sub>2</sub>)NH(CH<sub>2</sub>)<sub>d</sub> (d = 0-5), 3- or 4-guanylcyclohexyl, 1-guanyl-3- or -4-piperidinyl; m- or p-guanylphenyl; R4, R5, R6 = R1, OR1, NHR1, SR1, S(O)R1, CF3, CF2H, OCF3, OCF2H, halo, etc.; R7 = R1, CF3, CF2H, etc.] were prepared as enzyme inhibitors. Thus, N-[[2-hydroxy-3-(benzylsulfonylamino)-6-methylphenyl]acetyl]-L-argininal (in cyclol form) trifluoroacetate was prepared and showed IC<sub>50</sub> = 3.19 nM for inhibition of thrombin.

IT 225096-31-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

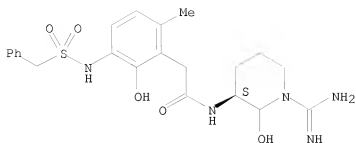
RN 225096-31-1 CAPLUS  
 CN Benzeneacetamide, N-[(3S)-1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]-2-hydroxy-6-methyl-3-[[[(phenylmethyl)sulfonyl]amino]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 225096-30-0  
 CMF C22 H29 N5 O5 S

Absolute stereochemistry.

10/923,271



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 225096-29-7P 225096-41-3P 225096-46-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

RN 225096-29-7 CAPLUS

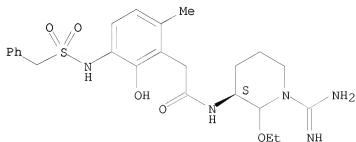
CN Benzeneacetamide, N-[(3S)-1-(aminoiminomethyl)-2-ethoxy-3-piperidinyl]-2-hydroxy-6-methyl-3-[(phenylmethyl)sulfonyl]amino]-, acetate (1:1) (CA INDEX NAME)

CM 1

CRN 225096-28-6

CMF C24 H33 N5 O5 S

Absolute stereochemistry.



10/923,271

CM 2

CRN 64-19-7

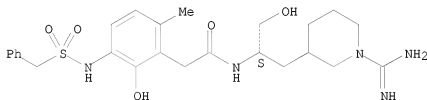
CMF C2 H4 O2



RN 225096-41-3 CAPLUS

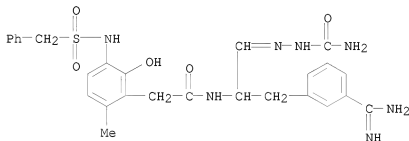
CN Benzeneacetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-(hydroxymethyl)ethyl]-2-hydroxy-6-methyl-3-[[ (phenylmethyl)sulfonyl]amino]-  
(CA INDEX NAME)

Absolute stereochemistry.



RN 225096-46-8 CAPLUS

CN Hydrazinecarboxamide, 2-[3-[3-(aminoiminomethyl)phenyl]-2-[[2-[2-hydroxy-6-methyl-3-[[ (phenylmethyl)sulfonyl]amino]phenyl]acetyl]amino]propylidene]-  
(CA INDEX NAME)



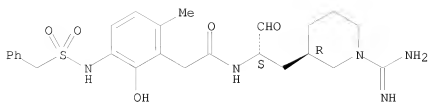
IT 225096-42-4P 225096-43-5P 225096-47-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

RN 225096-42-4 CAPLUS

CN Benzeneacetamide, N-[(1S)-2-[(3R)-1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[[ (phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

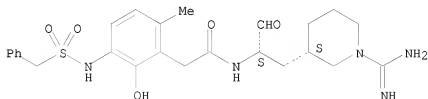
Absolute stereochemistry.



RN 225096-43-5 CAPLUS

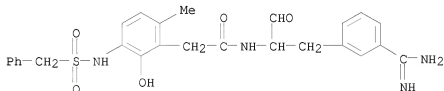
CN Benzeneacetamide, N-[(1S)-2-[(3S)-1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[(phenylmethyl)sulfonylamino]- (CA INDEX NAME)

Absolute stereochemistry.



RN 225096-47-9 CAPLUS

CN Benzeneacetamide, N-[2-[3-(aminoiminomethyl)phenyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[(phenylmethyl)sulfonylamino]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1989:154029 CAPLUS

DOCUMENT NUMBER: 110:154029

ORIGINAL REFERENCE NO.: 110:25463a, 25466a

TITLE: Preparation of 3-[(aroylamino)methyl]cephalosporins and analogs as antibiotics

INVENTOR(S): Bertrandie, Alain Michel; Jung, Frederic Henri; Bird, Thomas Geoffrey Colerick; Lohmann, Jean Jacques Marcel

PATENT ASSIGNEE(S): ICI Pharma, Fr.

SOURCE: Eur. Pat. Appl., 89 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

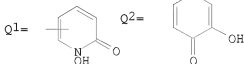
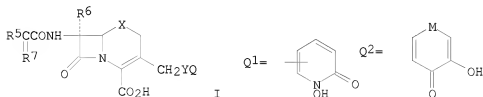
## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 267733	A2	19880518	EP 1987-309767	19871104 <--
EP 267733	A3	19891129		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8707987	A	19880831	ZA 1987-7987	19871023 <--
US 5017569	A	19910521	US 1987-117619	19871106 <--
FI 8704939	A	19880513	FI 1987-4939	19871109 <--
AU 8780926	A	19880519	AU 1987-80926	19871109 <--
AU 612990	B2	19910725		
DD 282691	A5	19900919	DD 1987-308889	19871110 <--
DK 8705918	A	19880513	DK 1987-5918	19871111 <--
NO 8704690	A	19880513	NO 1987-4690	19871111 <--
HU 46021	A2	19880928	HU 1987-5010	19871111 <--
HU 202541	B	19910328		
JP 63211288	A	19880902	JP 1987-284415	19871112 <--

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 110:154029

GI



AB The title compds. I [Q = C<sub>6</sub>H<sub>6</sub> ring (optionally fused to a further C<sub>6</sub>H<sub>6</sub> ring to form a naphthyl group, or optionally fused to a heterocyclic aromatic group) with substituents R<sub>1</sub> and R<sub>2</sub> which are ortho to one another, wherein R<sub>1</sub> = OH or an in vivo hydrolyzable ester thereof, and R<sub>2</sub> = OH, in vivo hydrolyzable ester thereof, CO<sub>2</sub>H, SO<sub>3</sub>H, CH<sub>2</sub>OH, etc., or Q = Q<sub>1</sub>, Q<sub>2</sub>; when Q is a C<sub>6</sub>H<sub>6</sub> ring fused to another C<sub>6</sub>H<sub>6</sub> ring, Q is optionally further substituted by C<sub>1</sub>-4 alkyl, halo, OH, cyano, etc.; M = O, NR<sub>3</sub>; R<sub>3</sub> = H, C<sub>1</sub>-4 alkyl; Y = NR<sub>4</sub>COY<sub>1</sub>, NR<sub>4</sub>SO<sub>2</sub>Y<sub>1</sub>, etc.; R<sub>4</sub> = H, (substituted) C<sub>1</sub>-4 alkyl, etc.; Y<sub>1</sub> = CO, (substituted) C<sub>2</sub>-4 alkenylene; X = S, O, methylene, sulfinyl; R<sub>5</sub> = (substituted) 2-aminothiazol-4-yl, 2-aminoxazol-4-yl, etc.; R<sub>6</sub> = H, MeO, NHCHO; R<sub>7</sub> = NOR<sub>8</sub> (with syn configuration about the double bond); R<sub>8</sub> = H, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-8 alkyl, C<sub>1</sub>-3alkyl-C<sub>3</sub>-6-cycloalkyl, etc.], were prepared as antibiotics. Deacylation of diphenylmethyl 7-(2-thienylacetamido)-3-(3,4-diacetoxybenzoyloxymethyl)ceph-3-em-4-carboxylate gave diphenylmethyl 7-amino-3-(3,4-diacetoxybenzoyloxymethyl)ceph-3-em-4-carboxylate (II). Acylation of II with 2-[(Z)-1-(tert-butoxycarbonyl)-1-methylethoxyimino]-2-(2-tritylaminothiazol-4-yl)acetic acid, followed by deprotection, gave 7-[2-(2-aminothiazol-4-yl)-2-(Z)-1-carboxy-1-methylethoxyimino]acetamido]-3-(3,4-dihydroxybenzoyloxymethyl)ceph-3-em-4-carboxylic acid (III). III in vitro exhibited a min. inhibitory concentration of 0.008 µg/mL against *Escherichia coli* DCO (A8341098).

IT 119733-84-5P

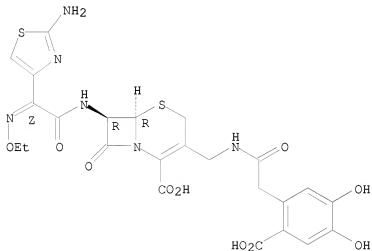
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of, as antibiotic)

RN 119733-84-5 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
7-[[[(2-amino-4-thiazolyl)(ethoxymino)acetyl]amino]-3-[[[(2-carboxy-4,5-dihydroxyphenyl)acetyl]amino]methyl]-8-oxo-, [6R-[6 $\alpha$ ,7 $\beta$ (Z)]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1988:221932 CAPLUS

DOCUMENT NUMBER: 108:221932

ORIGINAL REFERENCE NO.: 108:36443a,36446a

TITLE: Synthetic entry into yohimbinoid alkaloids and novel

synthesis of (±)-17-methoxyhexadehydroyohimbane

Pandit, Uttam Kumar; Das, Biswanath; Chatterjee, Asima

Dep. Chem., Univ. Coll. Sci., Calcutta, 700 009, India

Tetrahedron (1987), 43(18), 4235-9

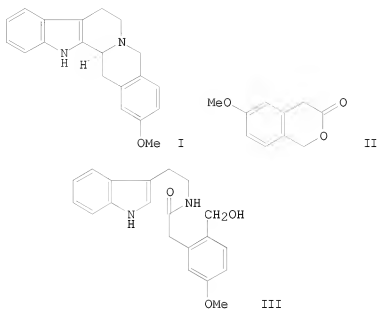
CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 108:221932

GI

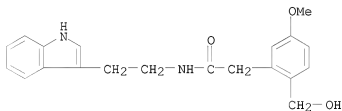


AB The title compound (I) was prepared from m-HOC<sub>6</sub>H<sub>4</sub>COMe via condensation of the lactone II with tryptamine and cyclization of the product III by polyphosphate ester.

IT 114547-02-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and intermol. cyclization of, methoxyhexadehydrochimbane from)

RN 114547-02-3 CAPLUS

CN Benzeneacetamide, 2-(hydroxymethyl)-N-[2-(1H-indol-3-yl)ethyl]-5-methoxy-  
(CA INDEX NAME)



L7 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:148061 CAPLUS

DOCUMENT NUMBER: 104:148061

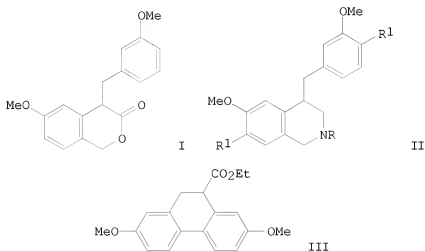
ORIGINAL REFERENCE NO.: 104:23416h,23417a

TITLE: Electrochemical oxidation of aromatic ethers. Part 10. Regioselectivity in the aryl-aryl coupling reactions of some 4-benzylisochroman-3-ones and benzyl-1,2,3,4-tetrahydroisquinolines

AUTHOR(S): Majeed, Amara J.; Patel, Premji J.; Sainsbury, Malcolm

CORPORATE SOURCE: Sch. Chem., Univ. Bath, Bath, BA2 7AY, UK

SOURCE: Journal of the Chemical Society, Perkin Transactions  
1: Organic and Bio-Organic Chemistry (1972-1999) (1985), (6), 1195-9  
CODEN: JCPRB4; ISSN: 0300-922X  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 104:148061  
GI



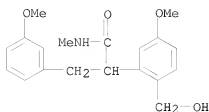
AB The anodic coupling reactions of 4-benzylisochromanone I and 4-benzyl-1,2,3,4-tetrahydroisoquinolines II (R = Me, R1 = H; R = Me, CO2Et, CHO, R1 = OMe) were studied and compared. In neutral media II gave products of coupling to C-1 and/or N-2, depending on the ring substituents. In acid solution, II gave isoaporphines, whereas the 1-benzyl analogs couple at C-8a to give morphinedienones. The different regioselectivities are due to inductive effects in the protonated bases. I also couples at C-8a but the resulting intermediate is unstable and reacts further with nucleophiles to give 24% 2,5-(OHC)(MeO)C6H3CH(CO2Me)CH2C6H4OMe-3 and 6.3% phenanthrene III.

IT 98748-62-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reduction of)

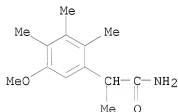
RN 98748-62-0 CAPLUS

CN Benzenepropanamide,  $\alpha$ -[2-(hydroxymethyl)-5-methoxyphenyl]-3-methoxy-N-methyl- (CA INDEX NAME)





L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 1969:96552 CAPLUS  
 DOCUMENT NUMBER: 70:96552  
 ORIGINAL REFERENCE NO.: 70:18029a,18032a  
 TITLE: Synthesis of sclerin  
 AUTHOR(S): Tokoroyama, Takashi; Maeda, S.; Nishikawa, Tomozo;  
 Kubota, Okuo  
 CORPORATE SOURCE: Osaka City Univ., Osaka, Japan  
 SOURCE: Tetrahedron (1969), 25(5), 1047-54  
 CODEN: TETRAB; ISSN: 0040-4020  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI For diagram(s), see printed CA Issue.  
 AB The synthesis of sclerin, which confirms the recently proposed structure  
 I, is described.  
 IT 13667-26-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 13667-26-0 CAPLUS  
 CN Benzeneacetamide, 5-methoxy- $\alpha$ ,2,3,4-tetramethyl- (CA INDEX NAME)



L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 1967:94748 CAPLUS  
 DOCUMENT NUMBER: 66:94748  
 ORIGINAL REFERENCE NO.: 66:17711a,17714a  
 TITLE: Synthesis of sclerin and sclerolide, metabolites of  
 Sclerotinia libertiana  
 AUTHOR(S): Kubota, Takashi; Tokoroyama, Takashi; Nishikawa,  
 Tomozo; Maeda, S.  
 CORPORATE SOURCE: Univ. Osaka, Osaka, Japan  
 SOURCE: Tetrahedron Letters (1967), (8), 745-8  
 CODEN: TELEAY; ISSN: 0040-4039  
 DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

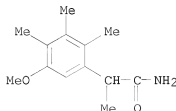
AB Hemimellitene (Marinc and Brown, CA 54, 9819f) submitted to Friedel-Crafts acetylation at 20° gave a 5:4 mixture of 2,3,4- and 3,4,5-trimethylacetophenone, separated by fractional distillation over a column.

Nitration of the former isomer gave 68% 2,3,4-trimethyl-5-nitroacetophenone (I, R = NO<sub>2</sub>) (II), m. 64-6°, along with small amts. of 2,3,4-trimethyl-5,6-dinitroacetophenone, m. 138-40°, and 2,3,4-trimethyl-5-nitrobenzoic acid, m. 176-7°. II was reduced with SnCl<sub>2</sub> to the aminoacetophenone I (R = NH<sub>2</sub>), m. 124-7°, and diazotized to give 53% I (R = OH) (III), m. 168°. III methylated with Me<sub>2</sub>SO<sub>4</sub> and K<sub>2</sub>CO<sub>3</sub> in Me<sub>2</sub>CO followed by reduction with LiAlH<sub>4</sub> gave 1-(1-hydroxyethyl)-5-methoxy-2,3,4-trimethylbenzene (IV), m. 68-9°, identical with a specimen from sclerin (V). IV treated with SOCl<sub>2</sub>, the chloride heated with NaCN in Me<sub>2</sub>SO at 120°, and the nitrile heated with aqueous 20% KOH and HOCH<sub>2</sub>CH<sub>2</sub>OH gave the nor-acid methyl ether (VI, R = H, R' = Me) (VII), m. 131° (amide m. 126-8°), obtained by milder hydrolysis. Demethylation of VII with HI gave the nor-acid VI (R = R' = H) (VIII), m. 128-30°. The identity of VII and VIII with the corresponding compds. from V was shown by ir spectral comparison. VII nitrated in Ac<sub>2</sub>O at -30° gave the nitro acid (IX, R = NO<sub>2</sub>), m. 208-9°, reduced catalytically in warm AcOH in the presence of Pd-C to give the 5-membered lactam (X), m. 211-13°, unsuitable for further transformation by the Sandmeyer reaction. VI (R = R' = Me) was chloromethylated and with concomitant lactonization gave 76% 6-membered lactone (XI), m. 115-16°. XI oxidized 24 hrs. with Jones reagent gave 30% IX (R = CO<sub>2</sub>H), converted by hot Ac<sub>2</sub>O to sclerin methyl ether (XII), m. 104-5°, demethylated with BBr<sub>3</sub> to racemic V. III nitrated in a mixture of AcOH and CCl<sub>4</sub> yielded 80% 3-hydroxy-4,5,6-trimethyl-2-nitroacetophenone (XIII, R = NO<sub>2</sub>, R' = H), m. 99-100°, converted to the Na salt and methylated with Me<sub>2</sub>SO<sub>4</sub> in refluxing C<sub>6</sub>H<sub>6</sub> to the 3-methoxy derivative XIII (R = NO<sub>2</sub>, R' = Me), m. 70-2°. Further transformation by treatment with SnCl<sub>2</sub> gave the amine XIII (R = NH<sub>2</sub>, R' = Me) (XIV), when as insufficient reduction led to formation of 7-methoxy-3,4,5,6-tetramethylantranil, m. 80°. Conversion of XIV by the Sandmeyer reaction gave XIII (R = CN, R' = Me), hydrolyzed in alkali to yield sclerolide Me ether (XV, R = Me), m. 145.5-6.5°, demethylated with HBr to sclerolide XV (R = H), identical with the natural product from *S. libertiana*.

IT 13667-26-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 13667-26-0 CAPLUS

CN Benzeneacetamide, 5-methoxy- $\alpha$ ,2,3,4-tetramethyl- (CA INDEX NAME)

10/923,271

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